REMARKS

Reconsideration of this application is requested in view of the foregoing amendments and following remarks.

I. Claim Amendments

Prior to entry of the foregoing amendment, claims 1-71 were pending.

Claims 18-21 are requested to be cancelled without disclaimer or prejudice to further prosecution on the merits

Claims 2-11, 55, and 61 currently are amended. Claims 2-11 and 61 are amended to correct typographical or grammatical errors. Claim 55 is amended effectively to incorporate the limitations of original claims 56-58 and to recite addition autoimmune diseases as disclosed in the specification at paragraph [0013].

After entry of the foregoing amendment, claims 1-17, and 22-71 are pending.

II. Claim Rejections – 35 U.S.C. § 112, first paragraph, "enablement"

Claims 55 and 59-63 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Claims 56-58 were not likewise rejected. Claim 55 has been amended to recite "[a] method of treating an autoimmune disease selected from a group consisting of multiple sclerosis, diabetes mellitus, lupus, host versus graft reaction, rejection of transplants, rheumatoid arthritis, and inflammatory bowel disease," as recited in claims 56-58 and as disclosed in the specification at paragraph [0013]. Therefore, the claim has been amended to recite a specific Markush group of autoimmune diseases which are enabled.

For these reasons, reconsideration and withdrawal of the rejection are requested.

III. Claim Rejections – 35 U.S.C. § 112, second paragraph, "indefiniteness"

Claims 2-11, 18 and 20 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to include a period. Claims 2-11 have been amended to include a period and claims 18 and 20 have been cancelled, obviating the rejection.

For these reasons, reconsideration and withdrawal of the rejection are requested.

IV. Non-Statutory Obviousness-Type Double Patenting (numerous patents)

Claims 1-71 stand rejected under the judicially created Doctrine of Obviousness Type Double Patenting as being unpatentable over claims of U.S. Patent Nos. 5,843,928; 6,392,071; 6,440,953; 6,482,812; 6,537,981; 6,696,431; 6,774,251; 6,806,262; 6,894,037; 6,992,074; 7,053,075; 7,115,594; 7,208,484; 7,214,670; 7,214,671; 7,232,810; 7,241,747; 7,241,909; and 7,244,719, in view of Bishop *et al.* (U.S. 5,972,917) or DeLuca *et al.* (WO 96/16035). The Office Action contends that each of these patents teaches 2-alkylidene-19-nor vitamin D compounds. Further, the Office Action contends that the claimed compounds differ from the compounds taught in each of these patents only in that the claimed compounds recite 18-nor derivatives, stating:

> The instant claims differ from the cited references in that they recite the 18-nor derivatives of the cited patents. However, (a) Bishop et al. (US 5,972,917) teaches an equivalent between hydrogen and methyl in the 18-position of vitamin derivatives (see col. 5, formula (II), definition of X) and (b) Deluca et al. teaches 18,19-dinor vitamin D derivatives show a preferential activity on intestinal calcium transport with reduced calcium mobilizing activity in bone (see page 5, lines 4-10). The compounds of Bishop and Deluca are taught to be useful in treating similar diseases such as cancer, psoriasis, multiple sclerosis, bone loss (see for example, '917, col. 9, line 54 – col. 10, line32; '035, page 5, lines 10-14; page 24, lines 30-35; pages 25-28, Biological activity of 18,19-dinor-vitamin D compounds). Based on the combined teachings of the cited references, the instant claims are rendered obvious.

The Applicants disagree that the presently claimed compounds are obviousness-type double patenting of the subject matter claimed in the cited patents.

First, regarding the Office Action's assertion that Bishop "teaches an equivalent between hydrogen and methyl at the 18-position of vitamin derivatives," what Bishop actually teaches is 1α-hydroxy-25-ene-vitamin D compounds. Bishop's vitamin D compounds are not 19-nor analogs and are not 2-alkylidene analogs, in contrast to the presently claimed compounds. Furthermore, Bishop's vitamin D compounds are characterized by low intestinal calcium transport, "thereby resulting in reduced or no hypercalcemia compared with similar dosing with know active vitamin D compounds such as 1α,25-dihydroxyvitamin D_3." (*See* Bishop, col. 4, lines 50-54.) In contrast, the presently claimed compounds are "characterized by relatively high intestinal calcium transport activity, i.e. similar to that of 1α,25-dihydroxyvitamin D_3, while also exhibiting relatively low activity, as compared to 1α,25-dihydroxyvitamin D_3, in their ability to mobilize calcium from bone." (*See* Specification, page 6, lines 1-6). Therefore, any teaching in Bishop regarding the equivalency of hydrogen and methyl at the C18-position relates to different vitamin D compounds (*i.e.*, 1α-hydroxy-25-ene-vitamin D compounds) having different biological activity (*i.e.*, low intestinal calcium transport) than the presently claimed compounds. As such, Bishop's teachings with respect to 1α-hydroxy-25-ene-vitamin D compounds would not be recognized as being applicable to the presently claimed 18,19-dinor, 2-alkylidene vitamin D compounds.

Furthermore, DeLuca *et al.* (WO 96/16035) (hereinafter "DeLuca WO"), teaches vitamin D analogs where hydrogen and methyl at the 18-position ***are not equivalent with respect to biological activity***. At FIG. 1, DeLuca WO indicates that 18,19-DINOR,1α,25$(OH)_2D_3$ is <u>more</u> effective than 1α,25$(OH)_2D_3$ at effecting differentiation of HL-60 cells, while 19-NOR,1α,25$(OH)_2D_3$ is <u>less</u> effective than 1α,25$(OH)_2D_3$ at effecting differentiation of HL-60 cells. As such, hydrogen and methyl at the 18-position of 19-nor compounds ***are not equivalent*** with respect to biological activity. At FIG. 2,

DeLuca WO indicates that 18-NOR,1α,25(OH)$_2$D$_3$ is less effective than 1α,25(OH)$_2$D$_3$ at binding to the 1,25-dihydroxyvitamin D pig intestinal nuclear receptor at relatively low concentrations. As such, hydrogen and methyl at the 18-position of 1α,25(OH)$_2$D$_3$ are not equivalent with respect to biological activity. Therefore, even if Bishop "teaches an equivalent between hydrogen and methyl at the 18-position of vitamin derivatives" as asserted in the Office Action, DeLuca WO teaches away from equivalency for hydrogen and methyl at the C18-position for 19-nor compounds and for 1α,25(OH)$_2$D$_3$.

For these reasons, one skilled in the art would not recognize that hydrogen and methyl are equivalent at the C18-position for all vitamin D compounds. Therefore, the claimed compounds having 18-nor, 19-nor, and 2-alkylidene modifications are not obviousness-type double patenting of the compounds claimed in the cited patents, which do not include 18-nor modifications. Reconsideration and withdrawal of the rejection are requested.

V. Non-Statutory Obviousness-Type Double Patenting (U.S. 7,238,681)

Claims 1, 22, 28-32, 34-38, 40-45, 47-53, 55-62, and 64-70 stand rejected under the judicially created Doctrine of Obviousness Type Double Patenting as being unpatentable over claims 1-48 and 59-67 of U.S. Patent No. 7,238,681 (hereinafter "the '681 Patent"). The Applicants have included herewith a properly executed Terminal Disclaimer to overcome the rejection.

VI. Non-Statutory Obviousness-Type Double Patenting (provisional)

Claims 1-71 stand provisionally rejected under the judicially created Doctrine of Obviousness Type Double Patenting as being unpatentable over claims of copending Applications Nos. 10/530,903; 10/544,163; 10/997,698 and 11/351,874 in view of Bishop and DeLuca WO. The rejection is a provisional obviousness type double patenting rejection because the conflicting claims in the applications have not in fact yet been

patented. Accordingly, if necessary, the Applicants will file a Terminal Disclaimer or cancel the allegedly overlapping claims to obviate the double patenting rejection upon the indication of allowable subject matter.

The Applicants traverse the rejection for the same reasons as stated above in Section IV. First, Bishop's teachings with respect to 1α-hydroxy-25-ene-vitamin D compounds would not be recognized as being applicable to the presently claimed 18,19-dinor, 2-alkylidene vitamin D compounds. Second, DeLuca WO discloses vitamin D analogs where hydrogen and methyl at the 18-position ***are not equivalent with respect to biological activity***.

For these reasons, one skilled in the art would not recognize that hydrogen and methyl are equivalent at the C18-position for all vitamin D compounds. Therefore, the claimed compounds having 18-nor, 19-nor, and 2-alkylidene modifications are not obviousness-type double patenting of the compounds claimed in the cited applications, which do not include 18-nor modifications. Reconsideration and withdrawal of the rejection are requested.

VII. Claim Rejections – 35 U.S.C. § 103(a)

Claims 18-21 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over DeLuca WO. Claims 18-21 have been cancelled, obviating the rejection.

VIII. Conclusion

An effort has been made to place this application in condition for allowance and such action is earnestly requested.

Respectfully submitted,
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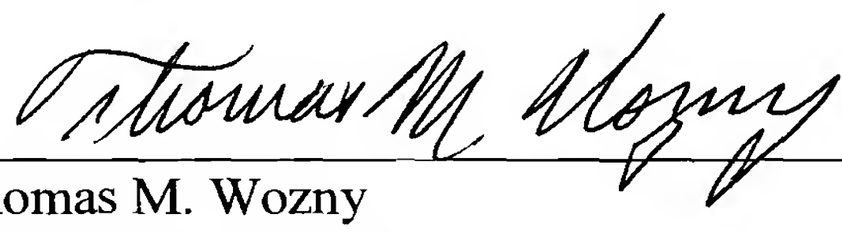

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